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Editorial

PLASTICS AND THEIR ADDITIVES REACHED THE BLOOD AND TISSUE SPACES: WHAT ARE THE POSSIBLE CONSEQUENCES?

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ABSTRACT: Microplastics, the tiny plastic particles are either manufactured for definite purposes or develop as the fragmented part of larger plastic materials. These can reach everywhere on the surface of our planet to do various detrimental impacts on humans and animals living on the land and in the sea, directly or after entering the food chain; on the overall biosphere as well as on the total environment by staying at a non-biodegradable state for centuries. The study of various health effects of microplastics is a comparatively new subject and different aspects of serious to very serious impacts of microplastics and their additives on health are becoming clear by such research. It is known that microplastics have already reached the tissues and become a reason for the death of fish and other edible or non-edible lives in the sea and water bodies. Possible effects of microplastics and their additive chemicals can be assumed from some experimental studies and the logical correlation of reports of such studies with the direct observations of the health status of living human beings. Recently it has been reported that microplastics and their additives already reached human blood and the placenta. Possible impacts of these chemicals on the endocrine system, their role in initiation and progression of different chronic diseases including cancers, effect on the brain, overall nervous system, and related behavioral changes as well as on the important organs of the body, like the liver, etc. are discussed in the light of published literature with an effort to search out the possible ways to reduce the load of microplastics and their additives inside our body to combat the incoming massacre.

Key words: Microplastics, Additives, Endocrine system, Cancers, Blood, Placenta, Health impacts.

We are now accustomed to plastics in almost every aspect of our life. Most of us already have some idea about the ill effects of plastics on our health and environment. Plastics cause pollution of the land, water bodies, rivers, and the sea along with the lives staying in their macro and micro-niches. More and more diverse health impacts of plastics on biota and health are being discovered day by day.

Synthetic plastic was first developed and used in 1907 in New York (Bakelite) (McCann 2021). The first plastic bag was used for health purposes (for collection and storage of blood) in 1950 (Walter 1951), and almost one decade later, the possible toxicity of plastic bags on human health was suspected (Gullbring 1964)!

Now we are using plastics for almost all household purposes. It is used in the pipelines and containers for storage and supply of drinking water and as some bags and packets for different purposes, from decorative packaging to storage and transportation of almost all industrial and household products, food, and drink items.

Plastics perhaps already reached everywhere on our planet. Plastic particles are found in the salt manufactured from the seawater and a good amount of plastics are present even in our feces (Campanale *et al.* 2020, Yee *et al.* 2021). Now it has been proved that the tiny plastic particles have already reached our blood and different tissue spaces (Braun *et al.* 2021, Leslie *et al.* 2022)!

Several articles are published on the toxicities of different plastics, their additives, etc. The detrimental effects of different plastics and their products on the sewage system, animal and bird health, marine life, the food chain, and the overall environment have also been discussed (UNEP 2018, Pattanayak 2018). Now, scientists are more worried about the health impacts of plastics!

The small-sized plastic particles are termed microplastics. Microplastics are some heterogeneous mixture of plastic materials of various shapes having sizes in the range of 0.1 to 5000 μm. The term nano-plastic is used to describe also some heterogeneous mixtures of further small-sized plastic mixtures, within the range of

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0.001- 0.1 μm. These micro and nano plastics are either originally manufactured in the industry or originate after fragmentation of the plastic materials of larger size or their debris (EFSA 2016). These tiny forms of plastics are capable to enter the body systems of man, animals, and birds of land and water. Though these can cause systemic effects after entry through the gut, lungs, and skin epithelia, their total and cumulative effects on health have not been studied thoroughly (Yee *et al.* 2021). Only the effects of the ingested plastics and their additives are to some extent studied. It is presumed that if micro-plastics and/or their additives can accumulate inside the body, they can influence the activities of different important internal organs or can reach the tissues and fluids of the body directly by leaching to bring various unknown dangerous impacts on health (Yee *et al.* 2021). Depending upon the available study reports, a brief analysis of the possible effects of plastics and their different additives inside the body system is targeted in the present article.

ENTRY AND ACTIVITY OF MICRO-PLASTICS INSIDE OUR BODY

A. Source and spread of microplastics

Several studies have already shown that micro-and nano-plastics are entering the human food chain in different ways. Direct ingestion of plastics with contaminated food or from plastic-made food plates or water/liquid containers, plastic coats of paper-made containers, etc. are some visible sources. Animals consume plastics directly even in their natural environment considering them wrongly as some food. Plastics can mix with our foods as some contamination during food production, processing, and/or through leaching from the plastic packaging materials used to hold or cover the food and drinks. These are so potent to spread that the micro- and nano-plastic particles have already been detected in honey, sugar, beer, etc. (Talsness *et al.* 2009, Pattanayak 2018, Li *et al.* 2021)!

Entry of plastics into the food chain can cause easy and high-speed transfer of it to us. Plastics are found in the digestive tract and different tissues of fishes, shrimps, mussels, and many other edible or non-edible marine species (European Commission 2011, USEPA 2016, Bisht and Negi 2020), as well as in birds (Leavers *et al.* 2019).

The nano-plastics generally develop due to the degradation of the microplastic wastes and can enter more easily into the human food chain due to their smaller size. Not only in food, micro and nano-plastics are also identified in tap, bottled, and spring water at different concentrations (Campanale *et al.* 2020, Flaws *et al.* 2020, Yee *et al.* 2021). As per reports of some experimental studies, they are also able to enter the bloodstream, lymphatic system, etc., and even can reach different tissues and organs (Wright and Kelly 2017, Kistler *et al.* 2019, Campanale *et al.* 2020).

B. Common micro-plastics and plastic additives in food and drinks and their activities

Several categories of plastics can come in contact with the food ingredients at their primary stage, during food preparation and processing, during post-processing packaging and distribution as well as from the plastic-made or plastic-coated plates, cups, or spoons during the serving of the food. Among the added plastics, polyester, polyvinyl chloride, polyolefins, polyvinylidene chloride, polyamide, polystyrene, ethylene vinyl alcohol, etc. are common (Raj 2005, Pattanayak 2018).

Microplastics have both physical and chemical effects on the blood and tissue spaces of different internal organs of the body. Not only the microplastics but all additives and colorants added with plastics can also easily mix with food and drinks if these come in contact with the plastics at any stage before the dietary intake. Among these, the most dangerous chemicals are all loosely bound synthetic color materials, bisphenol A and its derivatives, and different types of phthalates used in plastics (Talsness *et al.* 2009, Pattanayak 2018). Other important chemicals capable of causing serious health impacts are brominated flame retardants and lead heat stabilizers (Wright and Kelly 2017). In addition to chemical additives, plastic can also leach hazardous residual monomers. Among them, polyvinyl chloride, epoxy resins, polyurethanes, and styrene polymers are identified as plastics of the greatest concern in consideration of their impacts on health and the overall environment, as monomers of these plastics can show carcinogenic, mutagenic, or both of these effects (Wright and Kelly 2017).

i) Disruption of activities of the endocrine system

Some synthetic chemicals are having chemical structures almost similar to some hormones. After reaching the bloodstream and tissues, these can mimic the hormones and can disrupt both the functions of hormones in their effector tissues or organs and the production of these hormones by inducing the wrong feedback signal. There are chemicals having similarities with insulin, estrogen, progesterone, etc. Their actions can bring many detrimental health effects and can increase the risk of the development of many dangerous chronic diseases (https://www.niehs.nih.gov/health/topics/agents/endocrine/index.cfm).

Different plastic components can reach and accumulate inside our bodies from different sources, but all of them can act together. Many of these are having structural similarities with some important hormones or they can influence their functions in the body. Components like bisphenol A (BPA), phthalates, bis (2- ethylhexyl) phthalate (DEHP), polybrominated diphenyl ethers (PBDE), and tetra-bromo-bisphenol A (TBBPA) have been detected in the human body. These chemicals can alter the balance of our endocrine system (Talsness *et al.* 2009). These are having strong influence to initiate many hazardous diseases like Polycystic Ovarian Syndrome (PCOS) (Rutkowska and Rachoñ 2014, Wright and Kelly 2017). Bisphenol A, a plastic additive, can play some decisive roles in inducing infertility in males and females (Huo *et al.* 2015). Bisphenol A competes with estrogen and testosterone for their receptors, altering the balance of these hormones inside the body and so influencing reproductive health. Phthalates can function as some anti-androgenic agent inside the body. Polybrominated diphenyl ethers (PBDE) and tetra-bromo-bisphenol A (TBBPA) can disrupt the homeostasis of thyroid hormones. PBDEs can also act as some anti-androgenic agents (Talsness *et al.* 2009).

ii) Increasing the risk of chronic diseases

It has been observed that long-term exposure to microplastics can increase the risk of the development of diseases like Type 2 diabetes and even some cardiac diseases (Song *et al.* 2015).

There are associations between the high level of plastic additives like phthalates, dioxins, and bisphenol A in blood with several inflammatory diseases, improper glucose metabolism, increased chance of obesity, development of insulin resistance, and Type 2 diabetes (Lucas *et al.* 2022).

According to some research reports, exposure to microplastics in foods can cause more harmful effects on the body than continuous intake of unbalanced diets in consideration of risks for the development of chronic diseases (Lobstein and Brownell 2021).

iii) Disruption of immunity of the body and invitation of diseases like cancers

Microplastic exposure leads to improper gut health, weakening of the immunity status of the body, as well as an increase in the rate of development of different inflammatory conditions. Intestinal dysbiosis associated with detrimental effects on important intestinal structures like Peyer's patches can ultimately cause many compromises in the activities of the normal body immunity (Hirt and Body-Malapel 2020, Campanale *et al.* 2020). The immunological impact of microplastics is also dependent on the chemical composition of the plastics, as PET (polyethylene terephthalate) can act as a more harmful agent than PE (polyethylene). Some microplastics are having strong ability to act as carcinogens (*e.g*., butadiene, vinyl chloride, etc.), and some others are having strong power of mutagenicity (*e.g*., phenol, benzene, etc.) (Wright and Kelly 2017).

iv) Possible effects on the brain and other important organs

Observing the effects of the nano-particles of gold or titanium dioxide (which was considered as some inert chemical inside the body at their natural entry), it is assumed that micro- and nano-plastics may have neurotoxic health impacts of severe nature after reaching the brain. These can cause oxidative stress, induce cellular damage, and increase the chance of the development of different neuronal disorders. These can cause inhibition of the activity of acetylcholine esterase and alter the levels of the neurotransmitter and so can bring behavioral changes (Prust *et al.* 2020)!

Microplastics can reach different important organs through blood and may cause many serious health hazards. It may even affect important organs like the liver to cause problems in the normal functioning of those organs (Wright and Kelly 2017, Kistler *et al.* 2019, Campanale *et al.* 2020).

TOXICITY MECHANISMS OF MICROPLASTICS AND THEIR ADDITIVES

There may be several types of local and systematic effects of plastics inside the blood, tissue spaces, and the depositing organs. Depending on the available research reports, an assumption can be made about all such possible effects.

The Microfold (M) cells of the Peyer's patches of the intestinal wall can engulf particles of micrometer-sizes. These cells engage in the transport of luminal antigens to lymphoid follicles to initiate an immune response in the body. The microplastic particles above 2.5 um are of great concern as these can be engulfed by the M cells and further transported. These particles can reach the bloodstream and then can be carried to different organ tissues. Due to the unique surface chemistry, hydrophobicity as well as bio-persistent nature of the microplastics, the toxic effects are developed inside the body. The development and strength of the toxicity effects are dependent on the rate of accumulation and reaching some optimal gathering point of the microplastics to start

their toxic effects (Wright and Kelly 2017). The effects of acute or chronic exposure to micro and nano fragmentation of polystyrene were studied in human intestinal CCD-18Co cells. It is found that these can induce different metabolic changes by initiating oxidative stress, affecting the pathways of energy metabolism and different anabolic processes, and thus can be a risk factor for cancers (Bonanomi *et al.* 2022).

Important physical responses of microplastics are the development of inflammatory conditions, oxidative stress, genotoxicity, increased rate of apoptosis, and tissue necrosis. The lipid membrane of the cells may be destabilized by the microplastics which can affect the functioning of the cells and even increase the rate of cell death (apoptosis). Effect on energy and lipid metabolism invites some neurotoxic responses which ultimately bring some serious consequences. In response to sustained biological responses due to microplastics, a range of other detrimental outcomes may be expressed. Different important organs may face continuous tissue damage, then fibrosis, and up to carcinogenesis (Wright and Kelly 2017, Campanale *et al.* 2020)!

The chemical effects of the microplastics are depended on the chemical character of the microplastic monomers. Leaching of the unbound chemicals like color materials from the plastic utensils, the additives, unreacted residual monomers, and desorption of the associated hydrophobic organic contaminants (HOCs) are the main factors that act in this episode. The actual health impacts of many such chemicals are still unclear to the researchers.

Microplastics can leach different residual monomers in addition to the added chemical additives. Polyvinyl chloride (PVC), polyurethanes, epoxy resins, styrene polymers, etc. are considered chemicals of great concern in consideration of health and environmental effects of their monomers which are known to have mutagenic, carcinogenic, or both effects (Wright and Kelly 2017).

All plastics contain chemicals that act as reactive oxygen species (ROS) generators. It has a relationship with their history of polymerization and processing. Weathering of the microplastics generally leads to the formation of free radicals which can show toxic activities at the cellular level (Wright and Kelly 2017, Lavers *et al.* 2019).

So, the cellular uptake of microplastics ultimately can transport the endogenous materials and adhered contaminants inside the cells to cause further detrimental health effects (Wright and Kelly 2017, Campanale *et al.* 2020).

SOME RECENT STUDY REPORTS

A. Plastics in blood

In a recent study, the presence of different microplastics was analyzed in the blood samples of some donors. The study report showed the presence of various types of microplastics in the blood samples. Fifty (50) percent of blood samples showed the presence of polyethylene terephthalate (PET), thirty-six (36) percent samples contained polystyrene (PS), twenty-three (23) percent contained polyethylene (PE), and five (5) percent samples are having polymethyl methacrylate (PMMA). PET is generally used in the packaging of beverages, soft drinks, synthetic or semi-synthetic fruit juices, and water. PS is used in containers of different foods and also on disposable cups and plates. PE is used in the bags to carry grocery items, frozen foods, food carry containers and their lids, etc. PMMA is a transparent thermoplastic and so generally used as an alternative to glass.

From the studies, the presence of microplastics in blood and their possible source can be assumed. According to some researchers, our body shows a reaction actually to the sum of all cumulative microplastics and other xenobiotics entering through various routes like air (lung), water (drinking and absorption), foods, drinks (bottles containing beverages, water, synthetic or preservative added fruit juices, edible oils, and such other items), ingested personal care products (lipstick, nail polish), dental polymers, polymeric drugs, fragments of polymeric implants, tattoo ink residues, etc. (Leslie *et al.* 2022, Pattanayak 2022).

B. Plastics in the placenta

A study was performed on the collected placentas from physiological pregnancies that were analyzed for the presence of microplastics in them. Microplastic fragments of 5 to 10 μm size with spherical or irregular shapes were identified from both placentas of the fetal side and the maternal side as well as in the chorio-amniotic membranes. Some of the microplastics were chemically identified as pieces of stained polypropylene, a thermoplastic polymer. But from many others, identification of the pigments was only possible. The identified pigments are generally used in coatings, plasters, paints, finger paints, polymers, adhesives, and different personal care products like cosmetics (Ragusa *et al.* (2021)! In another study, presence of polyethylene, polysterine and polypropylene was detected from the placenta and meconium samples (Braun *et al.* 2021).

CONCLUSION

Plastics are extensively used for the last few decades and now the time has come to be rational in their use. Not only their effects are found on the life of animals, birds of the land and fishes, and other marine animals, plastics reached the food chain and even in our blood and organ tissues. The main entry of plastics happens through the oral route, so it can be reduced to a large extent through personal consciousness. Limiting consumption of processed foods by depending more on traditional home-made foods, choosing eco-friendly food packaging by use of paper, jute, or cotton bags in packaging; replacing plastic water bottles, cups, food plates, utensils, etc. with suitable biodegradable natural materials or materials like glass or stainless steel, etc., we can slow down their environmental deposition and reduce the concentration of micro and nano plastics and/or their additives in our blood and tissue spaces.

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